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| EXAMINER | |
|---|---|
| LE, EMILY M | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/733,488 | ILAN ET AL. | |
| | Examiner | Art Unit | |
| | Emily Le | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08/23/06+12/15/06*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *50-52 and 55-62* is/are pending in the application.

4a) Of the above claim(s) *61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-52, 55-60 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08/23/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of Claims*

1. Line 1, page 4 of Applicant's 12/15/2006 submission, Applicant submits that claims "1-62 are currently pending in this application." However, it should be noted that it is claims 50-52 and 55-62 that are pending. Claims 1-49 and 53-54 have been cancelled by Applicant. Claim 61 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 08/02/2005. Claims 50-52, 55-60 and 62 are under examination.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 50-52, 55-60 and 62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response to the rejection, Application amended the claims to limit the mammalian metabolite to a glycolipid and the disease being treated with the claimed method includes those having a defect in an immune response as part of the pathogenesis of the disease. Applicant additionally submits that the specification is

enabling for "one skilled in the art to administer a glycolipid for the purpose of modulating at least one immune parameter, such as IFN-gamma, for example": [First full line, page j8 of Applicant's 08/23/2006 submission.] To support Applicant's position, Applicant cites pages 13-15 of the specification as passages that offer guidance to those skilled in the art with regard to both the specific compounds as well as specific diseases to be treated with the claimed invention. Applicant also submits that immunoparameters or markers associated with particular immune disease are well known in the art, and the skilled artisan would readily use this knowledge to practice the claimed invention. Applicant further submits that the specification provides evidence that specific immune parameters are modulated in response to a metabolite, such as glycolipid. To support this submission, Applicant directs the Office's attention to Figures 1-6, which illustrates the results of assays leading to T-cell proliferation and changes in IFN-gamma, IL-4 and peripheral NKT lymphocytes. Lastly, Applicant submits that these assays and figures demonstrate that the presence of an increased level of metabolite has led to significant changes in the immune profile of these subjects. Applicant further concludes that, surprisingly, when this condition was accompanied by another immune system challenge, HCV infection, there was significant impact on the immune profile of the HCV positive subjects compared to the subjects that lacked elevation of the metabolite.

Applicant's submission has been carefully considered, however, it remains that the specification is not enabling for the claimed invention. The submission provided by Applicant is not commensurate in scope with the claimed invention. The claimed

invention is directed at the treatment of diseases, rather than modulation of immune responses. Had the claimed invention been limited to a method of modulating the immune response, then the Office would agree with Applicant that the specification has provided and demonstrated a sufficiently enabling disclosure for the modulation of the immune system. However, unfortunately, that is not the case. The claimed invention remains to be a method of treating diseases. In the instant case, Applicant has not provided any working examples that evidence or demonstrate that the administration of a glycolipid or any mammalian metabolite is indeed effective in providing a therapeutic response against diseases. As mentioned in the previous office action, the specification is defective in this regard. The specification does not provide an enabling disclosure through any working examples. Furthermore, the specification does not provide any guidance or direction regarding the claimed invention. While it is noted that Applicant submits that pages 13-15 of the specification offer guidance to those skilled in the art with regard to both the specific compounds as well as specific diseases to be treated with the claimed invention; however, it should be noted that these are merely assertions or suggestions of use. These assertions are not supported by any evidence.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In Genentech *Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.,* 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24

(CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The nature of the invention is directed at the administration of a glycolipid to treat diseases in a subject.

With the exception of claim 60, the claims are not limited to any particular diseases, just those that have a defect in an immune response as part of the pathogenesis of the disease. Hence, it is found that the full breadth of the claims encompasses a method for treating all diseases, including viral, bacterial, fungal and parasitic infections; and cancer. The most limiting breadth of the claimed invention is the invention recited in claim 60, which limits the disease to HCV.

Yet, the specification has not set forth any evidence demonstrating that the administration of glycolipids treats any disease. Nor has the specification set forth any guidance or direction relating to the therapeutic use of glycolipids to treat any disease. All that is present in the disclosure is suggestions and assertions of use, however, there does not exist any evidence demonstrating the effective use of glycolipids to treat any disease. The specification is fatally defective for the claimed invention.

As mentioned in the previous office action, all that is noted in the specification is an association between the Gaucher's disease and Hepatitis C virus infection. In the specification, Applicant notes that subjects diagnosed with Gaucher's disease and HCV infection have an immune profile that is different from those diagnosed with only Gaucher's disease, all of which is summarized in Figures 1-6 in the specification. Specifically, Applicant notes the following: i) HCV specific T cell proliferation and the percent of peripheral natural killer T lymphocytes are less in subjects diagnosed with both Gaucher's disease and HCV infection compared to those diagnosed with only Gaucher's disease; and ii) the level of interferon gamma, interleukin-10, interleukin-4 observed in subjects diagnosed with both Gaucher's disease and HCV are higher than those diagnosed with only Gaucher's disease. In the instant, at the very best, the specification sets forth a nexus among various immune parameters, HCV and Gaucher's disease. The specification does not set forth any guidance that would bridge the gap between the observations made by Applicant in the specification and the claimed invention. There is no information provided in the specification pertaining to the type of immune parameter that should be modulated to treat a disease. There is no information provided in the specification regarding the specific immune parameter that a particular metabolite modulates. No such information or guidance is provided in the specification. The skilled artisan cannot rely on the disclosure set forth in the specification to reasonably practice the invention without an undue burden of experimentation.

In order for the skilled artisan to successfully practice the claimed invention, the skilled artisan must ascertain information pertaining to the type of immunoparameter that should be modulated to treat a disease, and the specific metabolite, glycolipid, that modulates the immunoparameter required for the treatment of the disease. In the instant, the attainment of such information would surely bridge the gap between the use of metabolites and its use in treating a disease. However, the information acquisition process would undeniably be an undoubtedly laborious task that includes both undue and blind experimentations. The skilled artisan would have to unduly and blindly experiment with each known disease, immunoparameters and metabolites to establish a relevance each of the listed variables has over the other. At the time of filing of the instant patent application, the art recognizes that there are approximately 800 to 2000 different metabolites assayed in human subjects.[1] Matching the large number of metabolites known to exist in humans is thousands of diseases, not to mention numerous immunoparameters. A search of the literature renders that there are more than 4000 different diseases, as evidenced by the alphabetical listing of diseases compiled by Karolinska Institutet. Karolinska Institutet summarizes that the 4000 plus diseases fall into the following categories: Bacterial Infections and Mycoses, Virus Diseases, Parasitic Diseases, Neoplasms (Cancer), Musculoskeletal Diseases, Digestive System Diseases, Stomatognathic Diseases, Respiratory Tract Diseases, Otorhinolaryngologic Diseases, Nervous System Diseases, Eye Diseases, Urologic and Male Genital Diseases, Female Genital Diseases and Pregnancy Complications,

[1] Beecher W.C., Metabolic Profiling: Its Role in Biomarker Discovery and Gene Function Analysis,

Cardiovascular Diseases, Hemic and Lymphatic Diseases, Congenital, Hereditary, and Neonatal Diseases and Abnormalities, Skin and Connective Tissue Diseases, Nutritional and Metabolic Diseases, Endocrine Diseases, Immunologic Diseases, Disorders of Environmental Origin/Poisoning, Animal Diseases, Pathological Conditions, Signs and Symptoms, Behavior and Behavior Mechanisms, and Mental Disorders. (A listing of diseases is attached. The complete listing of diseases is retrieved from http://www.mic.ki.se/Diseases/Alphalist.html)

With such a large abundance of information to mine and analyze, the quantity of experimentation that the skilled artisan would have to conduct is endless. And the imposition of endless experiments would unarguably be an undue burden for the skilled artisan. Hence, the claims are rejected under 112, 1st paragraph for failure to provide an enabling disclosure.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F. 2d 1557, 1562, 27 USPQ 2d 1510, 1513 (Fed. Cir. 1993).

***Double Patenting***

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

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Chapter 17: The human metabolome. *Kluwer Academic, 2003.*

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claim 55 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 106 of copending Application No. 10/675980.

In response to the rejection, it is noted that Applicant has requested this rejection be held in abeyance.

Applicant's request is noted, and will be held in abeyance until the indication of allowable subject matter. However, it should be noted that until the rejection is properly addressed, the rejection is maintained.

Claim 55 of the instant application is directed at a method of for treating a disease in a mammalian subject comprising administering to said subject an effective amount of a mammalian metabolite to modulate or change at least one component in the immune system of said subject, wherein the mammalian metabolite is a glycolipid comprising a monosaccharide ceramide.

Claim 106 of the conflicting patent application is directed at a method for treating a disease in a mammalian subject comprising administering to said subject an effective amount of an intermediary metabolite to modulate or change at least one component in the immune system of said subject, wherein the intermediary metabolite is glucosylceramide or galactosylceramide.

The difference between the two claims is that claim 106 of the conflicting recites the use of a glucosylceramide or galactosylceramide; whereas, claim 55 is directed at the use of a glycolipid comprising a monosaccharide ceramide.

In the instant, the genus glycolipid comprising a monosaccharide ceramide recited in claim 55 is generic for the species glucosylceramide and galactosylceramide. That is, claim 106 of the conflicting patent application falls entirely within the scope of claim 55. Claim 55 is anticipated by claim 106 of the conflicting patent application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Conclusion***

6. No claims are allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bruce R. Campell/
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/E.Le/